

REMARKS

Applicants' invention provides an abuse-resistant composition that contains a water soluble active ingredient, susceptible to user abuse, and that surrounds such ingredient with a water insoluble matrix, which retains its water protecting functionality despite being subject to mechanical stress, such as crushing, prior to ingestion, which stress would otherwise act to accelerate the aqueous release of the active in prior art compositions.

Discussion of the Amendment

Claim 1 has been amended to incorporate the recitations of now cancelled claims 2, 3, 6 and 8. Amended claim 1 now more precisely defines the active as "water soluble", and the water insoluble coating material as comprising the matrix in which the active is contained (support is found in original claims 2, 3, and 6), as well as the mechanical stress as being "compressing, fracturing, tumbling, rolling, or milling said matrix before coming in contact with water ". Support is found on page 6, lines 21-23.

Additionally, claim 1 defines the active release retardant property as that which "increases the aqueous dissolution of said active water soluble compound in said composition by less than about 15% of said pharmaceutically effective amount in the first hour, and does not substantially modify the dissolution rate of said water soluble compound thereafter". Support is found in original claim 8.

Claim 9 is amended to more precisely define the mechanical stress as "crushing" before coming in contact with water. Support is found in original claim 10.

New claim 25 is dependant on claim 1 and further defines a preferred process to form the abuse-resistant matrix: "pressure-pulse is applied to a flowable mixture of said coating material and said active water soluble compound to form a pressure-treated matrix". Support is found in original withdrawn claims 12 and 13.

New claim 26 is dependent on claim 25 and further recites the preferred microsphere forming process: “said pressure-treated matrix is spray cooled to form microspheres”. Exemplary support is found on page 17, lines 3-6.

Discussion of the Examiner’s Art Rejection

Claims 1-11 and 24 stand rejected under 35 USC Section 102(b) over US Patent No. 6228863 (*Palermo et al.*).

Applicants respectfully traverse the Examiner’s rejection.

Palermo et al. teach the formulation of a myriad of sustained release compositions, but direct their principle teaching to the requirement for a second ingredient, an opioid antagonist, to reduce the abuse potential of the composition:

The invention relates in part to a method of reducing the abuse potential of an oral dosage form of an opioid analgesic, wherein an analgesically effective amount of an orally active opioid agonist is combined with an opioid antagonist into an oral dosage form which would require at least a two-step extraction process to be separated from the opioid agonist, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist and administered parenterally. (*Palermo et al.*, Abstract)

Palermo et al. focus on frustrating the abuser’s attempts at dissolution by requiring a second extraction step. *Palermo et al.*’s remaining teachings are standard for the art of sustained release compositions. Nowhere do *Palermo et al.* disclose or suggest a means for retarding the aqueous dissolution of the active if the composition is abused.

Applicants’ invention frustrates the abuser by setting up a formulation barrier that inhibits aqueous dissolution in the first instance, and prevents the abuser from achieving a “high” by the common method of crushing the composition for nasal inhalation. Applicants’ composition is a

poor candidate for achieving a high by crushing and nasal inhalation, as the active is effectively prevented from being rapidly released by such methods.

Claim 1 now incorporates the recitations of original claim 8, which the Examiner recognized recites the application of “mechanical stress”. Applicants have further recited the types of stress that an abuser may apply to the composition, as disclosed on page 6 of the original specification, “compressing, fracturing, tumbling, rolling, or milling said matrix before coming in contact with water “. Claim 1 now clearly distinguishes over the types of mechanical stress, such as peristalsis after ingestion, that are normal and expected for the proper use of such compositions.

Applicants submit that the claims as amended distinguish patentably over *Palermo et al.* and are in condition for allowance.

A favorable action on the merits is requested respectfully.

Respectfully submitted,

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